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EXAMINER	
BOESEN, AGNIESZKA	
ART UNIT	PAPER NUMBER
1648	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/584,934	SCHUBERT, ULRICH	
	Examiner	Art Unit	
	AGNIESZKA BOESEN	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 September 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-38* is/are pending in the application.

4a) Of the above claim(s) *1-22,33,34,37 and 38* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22-32, 35 and 36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Non-Final Office Action is responsive to the communication received 3/26/2009 and 9/14/2009.

Election/Restrictions

Applicant's election without traverse of group II, claims 22-32, 35 and 36 is acknowledged. Claims 1-22, 33, 34 and 37-38 are withdrawn because the claims are drawn to the non-elected invention.

Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 22-32, 35 and 36 are under examination in this Office Action.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 22-32, 35 and 36 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make, and/or use the invention.

In making a determination as to whether an application has met the requirements for enablement under 35 U.S.C. 112 ¶ 1, the courts have put forth a series of factors. See, In re Wands, 8 USPQ2d 1400, at 1404 (CAFC 1988). The factors that may be considered include (1)

the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. Id. While it is not essential that every factor be examined in detail, those factors deemed most relevant should be considered. In the present case, the factors deemed relevant are those of the amount of direction and the working examples provided, that quantity of experimentation necessary, the (un)predictability of the art, and the breadth of the claims.

Claims are drawn to a method for inhibition of assembly and maturation of virus structure proteins in an organism comprising administering a pharmaceutical preparation comprising an inhibitor of cellular chaperones or chemical chaperones. The present specification discloses that that the inhibitors of the chaperones are Sodium-4-phenylbutyrate (4-PBA), which blocks Hsc70, and Herbimycin A, which blocks Hsp90 Geldanamycin and Deoxyspergualin, which block the activities of the proteins of the Hsp90 and the Hsp/Hsc70 families (see 0007 and 0009).

The specification contemplates treatment and prevention of viral infections including HIV infection, HCV, Ebola virus and other (Specification [0013] and [0074]).

[0013] Fields of application are both in the treatment as well as in the prevention of viral infections. Agents for the treatment of various virus infections which contain chemical chaperones in pharmaceutical preparations as effective inhibitors of folding enzymes were subsequently developed. The newly developed drugs developed in accordance with the invention are suitable for the treatment, therapy and inhibition of infections with various human pathogenic and also animal pathogenic viruses. The focus of the invention lies on pathogenic agents causing chronic infectious diseases, such as AIDS (HIV-1 and HIV-2), hepatitis (HCV and HBV), the causative agent of the "Severe Acute Respiratory Syndrome" (SARS), the SRAS-CoV (Corona virus), the smallpox, the causative agents of the viral hemorrhagic fever (VHF), such as the Ebola -viruses as a representative of the Filoviridae family; the causative agents of flu, such as the Influenza-A -Virus.

[0074] The inhibition of the following retroviruses is possible: Spuma -viruses, Mammalian-C-Typ-Onco -viruses, BLV (Bovine Leukemia Virus), HTLV (Human T-Cell Leukaemia Virus), leukaemia viruses, RSV (Rous Sarcoma Virus) or lent viruses. Examples for leukaemia viruses are BLV, HTLV-I or HTLV-II. Examples for lent viruses are Humans Immune Deficiency Virus Type 1 (HIV-1), Humans Immune Deficiency Virus Type 2 (HIV-2), Simian Immune Deficiency Virus (SIV), Feline Immune Deficiency Virus (FIV) or Bovine Immune Deficiency Virus (BIV). [0078] A prevention of a disease outbreak and a reduction in the level of the spread of the infection in the organism (reduction of the "viral load") of symptom-free HIV-1/HIV-2 seropostive and HIV-1/HIV-2 infected individuals are empirically also possible. Furthermore inhibitors of cellular chaperones, or chemical chaperones, can be used for the treatment/therapy/prevention of HIV-induced demence, especially for the prevention of an HIV-infection of the neurons, glia and endothelial cells in capillaries of the brain. Another use is the interference with the establishment of a systemic HIV-1/HIV-2 infection immediately after coming in contact with the infectious virus (for example due to a pinprick injury with HIV-contaminated blood or blood products).

The claims are broadly drawn to methods of inhibiting assembly of any virus comprising administering a pharmaceutical preparation comprising administering any inhibitor of cellular or chemical chaperones. The claims are rejected because the specification does not provide sufficient enabling disclosure for the large genus of viruses, the genus of inhibitors of cellular or chemical chaperones or the phrase “pharmaceutical preparation”. It is noted that the phrase "pharmaceutical preparation" implies a composition for active therapy in humans. However Applicants specification has not established any pharmaceutically applicable doses of the chemical chaperones that are used in the claimed methods. The working examples provided in the specification contemplate treatment of Flaviviruses, retroviruses and SARS virus with the inhibitors of cellular chaperones (Example 1-8).

EXAMPLE 1 [0101] The treatment of Flaviviridae-infected cell cultures with moderate concentrations of inhibitors of cellular chaperones, or of chemical chaperones, drastically reduces the release and spread infectious progeny viruses.

EXAMPLE 2 [0102] The treatment of Flaviviridae-infected cells with inhibitors of cellular chaperones, or with chemical chaperones, leads to differences in the number of in infected cells, detectable virus particles, to changes of the proportion of complete to non-complete virions, as well as to changes in the morphology of secreted progeny viruses.

EXAMPLE 3 [0103] Inhibitors of cellular chaperones, or chemical chaperones, have inhibiting processes and modification of the structure proteins of BVDV and HCV.

EXAMPLE 4 [0104] The treatment of HIV-1 infected cells with inhibitors of cellular chaperones, or with chemical chaperones, reduces the infectivity of released virus particles.

EXAMPLE 5 [0105] Electron microscopic analysis of HIV-1 infected MT-4-cells after the treatment with inhibitors of cellular chaperones, or with chemical chaperones.

EXAMPLE 6 [0106] Inhibitors of cellular chaperones, or chemical chaperones, interfere with the Gag-processing and release of virus from infected T-cell cultures and transfected HeLa-cells.

EXAMPLE 7 [0107] Inhibitors of cellular chaperones, or chemical chaperones interfere with HIV-1 replication in cell cultures.

EXAMPLE 8 [0108] Inhibition of the replication of SARS-CoV in Vero-cells through inhibitors of cellular chaperones, or chemical chaperones.

However the specification does not provide any evidence that the replication of any of the viruses contemplated in the specification can be inhibited by administering the inhibitors of cellular chaperones in a subject. The art teaches that the replication of cellular chaperones such as Hsp90 is inhibited with geldanamycin *in vitro* and that Hsp90 is important for the replication of vaccinia virus (Hung, Journal of Virology, 2002, Vol.76 and Waxman (WO 02/07761 A1). The art does not teach inhibition of HIV or Ebola virus replication in humans administered inhibitors of cellular chaperones. Considering the large genus of viruses and possible chemical compositions, it would have been an undue amount of experimentation to practice the claimed methods. Furthermore, regarding in vivo methods, which rely on generally unpredictable mechanisms, “The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The "amount of guidance or

direction" refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling. >See, e.g., *Chiron Corp. v. Genentech Inc.*, 363 F.3d 1247, 1254, 70 USPQ2d 1321, 1326 (Fed. Cir. 2004) ("Nascent technology, however, must be enabled with a 'specific and useful teaching.' The law requires an enabling disclosure for nascent technology because a person of ordinary skill in the art has little or no knowledge independent from the patentee's instruction (MPEP 2164.03).

Further, in Rasmusson v. SmithKlineBeecham Corp., 75 USPQ2d 1297-1303 (CAFC 2005). The court states, "If mere plausibility were the test for enablement under section 112, applicants could obtain patent rights to "inventions" consisting of little more than respectable guesses as to the likelihood of their success. When one of the guesses later proved true, the inventor would be rewarded the spoils of the party who demonstrated the method actually worked. That scenario is not consistent with the statutory requirement that the inventor enable an invention rather than merely proposing an unproved hypothesis."

As discussed above undue experimentation would be required to practice the claimed invention. In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in specification, and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 22-32, 35 and 36 are rejected under 35 U.S.C. 102(b) as being anticipated by Waxman (WO 02/07761 A1).

Claims are drawn to a method for inhibition of assembly and maturation of virus structure proteins in an organism comprising administering a pharmaceutical preparation comprising an inhibitor of cellular chaperones or chemical chaperones. The present specification discloses that that the inhibitor of the chaperones are Sodium-4-phenylbutyrate (4-PBA), which blocks Hsc70, and Herbimycin A, which blocks Hsp90 Geldanamycin and Deoxyspergualin, which block the activities of the proteins of the Hsp90 and the Hsp/Hsc70 families (see 0007 and 0009).

[0007] Further inhibitors of molecular chaperones are Sodium-4-phenylbutyrate (4-PBA), which blocks Hsc70, and Herbimycin A, which blocks Hsp90.
[0009] The goal of the invention was solved by application of inhibitors of protein folding enzymes. Especially inhibitors of cellular chaperones, such as the heat shock proteins (hsp) have been used. Belonging to this category are agents which hinder the activities of the heat shock proteins Hsp40, Hsp70, Hsp90, Hsp27 and Hsc70, for example the substances Geldanamycin and Deoxyspergualin, which block the activities of the proteins of the Hsp90 and the Hsp/Hsc70 families.

[0010] Agents for the treatment of various virus infections were subsequently developed which contained inhibitors that blocked molecular chaperones as active components. Such substances include Geldanamycin, Deoxyspergualin, 4-PBA or Herbimycin A. Substances in form of chemical chaperones are also used that regulate, disturb and block conformation and folding of viral proteins. Such substances include Glycerol, Trimethylamins, Betain, Trehalose or deuterized water (D.sub.2O).

Waxman discloses a method for inhibiting Hepatitis C virus (which belongs to a Flaviviridae family) processing and replication, comprising administering inhibitors of cellular chaperones, wherein the inhibitor is geldanamycin, herbimyin A or radiciciol (see claims 1-18, and Examples 1-7).

Thus by this disclosure Waxman anticipates the present claims.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 22-32, 35 and 36 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-24 of copending Application No. 12/325,598. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of this and the copending Application are

drawn to a method of inhibition of the assembly of the virus structure proteins comprising administering an inhibitor of a cellular chaperone.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to AGNIESZKA BOESEN whose telephone number is (571)272-8035. The examiner can normally be reached on Monday through Friday from 9:00 AM to 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached at 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Agnieszka Boesen/
Examiner, Art Unit 1648